Pesticide Registration (PR) Notice 96-8

October 31, 1996

PESTICIDE REGULATION (PR) NOTICE 96-8

NOTICE TO MANUFACTURERS, FORMULATORS, PRODUCERS AND REGISTRANTS OF PESTICIDE PRODUCTS

ATTENTION: Persons Responsible for Registration of Pesticide Products

SUBJECT: Toxicologically Significant Levels of Pesticide Active Ingredients

This notice sets out the Environmental Protection Agency's (EPA's) interpretation of the term "toxicologically significant" as it applies to contaminants in pesticide products that are also pesticide active ingredients (AIs). This notice provides risk-based concentration levels of such contaminants that will generally be considered toxicologically significant. These concentrations are defined according to the type of pesticide that is contaminated and the pesticide category of the contaminant. As provided by regulation, registrants must report to EPA contamination exceeding toxicologically significant levels. This Notice sets out procedures for reporting such contamination.

The following contamination scenarios are excluded from this notice: (1) rodenticides as a contaminant and/or as the contaminated product; (2) microbial and biochemical pesticides that are manufactured in fermentors and that are contaminated by active microbial pesticide ingredients; and (3) plant-pesticides that are contaminated with other active plant-pesticide ingredients. EPA would like to clarify that the Agency's previous position on toxicologically significant levels of impurities that are also AIs would apply to pesticides that are exempt from this notice. In other words, any level of a contaminant in these three exempted categories would be considered potentially toxicologically significant and must be reported to EPA.

I. BACKGROUND

EPA requires all impurities of toxicological significance to be reported and accepted as part of product registration (40 CFR 158.167). EPA also requires that registrants propose upper certified limits for toxicologically significant impurities in technical grade active ingredients or products produced by an integrated system (40 CFR 158.175), and may require upper certified limits for other impurities.

At the time EPA promulgated these regulations it did not set quantitative criteria for determining whether an impurity is toxicologically significant. Rather, EPA has taken the position that any level of an active ingredient that is an impurity or contaminant in another product is potentially toxicologically significant and must be reported to the Agency. Failure to report such an impurity is a violation of FIFRA section 12(a)(1)(C) (composition of the product differs from that registered with the Agency).

The Agency did make clear at the time it promulgated its current reporting regulations that its interpretation of the term toxicologically significant could be subject to further refinement to the extent new information on impurities was available to the Agency. Based on the analysis conducted during the development of this notice, the Agency has now determined that for certain pesticides (see section IV below) it can establish generally applicable quantitative criteria for determining the toxicological significance of contaminants that are also active ingredients. For this reason, EPA is today further refining its interpretation of the term "toxicologically significant."

In Section IV of this notice, EPA is setting risk-based levels at which active ingredients that are contaminants will generally be considered "toxicologically significant." For the purposes of this notice, a contaminant is defined as an active ingredient that is not accurately listed on the product's confidential statement of formula or listed in the discussion of impurities. This notice addresses only impurities that are also active ingredients; EPA's position on other impurities has not changed.

Additionally, nothing in this notice changes the conditions outlined in the Bulk Pesticides Enforcement Policy (Bulk Policy) dated July 11, 1977 and amended on March 4,

1991. The Bulk Policy is an important part of applying the 40 CFR Part 158 standards to bulk pesticides at repackaging/refilling establishments (often retail dealers). Specifically, EPA's position that both parties (the registrant and the repackager) are accountable for the integrity of the product as set out in the Bulk Policy remains the same.

II. OBJECTIVES

EPA determined that this interpretation on cross contamination should:

- Recognize that cross contamination is a reality, and that not all cross contamination is problematical;
- Set a clear standard that can be readily applied by EPA/States and the regulated industry alike;
- Ensure that allowable cross contamination does not pose unreasonable adverse effects;
- Minimize the paperwork burden for EPA and registrants;
- Maintain accountability for the product from the registrant to the end user; and
- Not preclude marketplace/private solutions to correct problems that do arise.

III.APPROACH

EPA decided that a risk-based approach would most likely meet these objectives.

EPA considered the risks for several endpoints, including human health, adulterated food, contamination of ground water, and ecological effects to determine which endpoints would be most sensitive to cross contamination and what levels of cross contamination could be tolerated and remain generally protective of human health and the environment. For each endpoint, an analysis was done to evaluate a reasonable worst case scenario or a range of potential scenarios to see if an overall, generally protective contaminant concentration could be determined. EPA grouped contaminants and pesticides into different categories (see the table in section IV) to yield a scheme of toxicologically significant concentrations.

The following end points were considered. In most cases phytotoxicity to the target plants is the most sensitive endpoint and, therefore, the limiting factor in determining toxicological significance.

Human health effects. Because cross contamination caused by a specific AI is most likely an intermittent event, short-term exposure is most likely. Therefore, EPA focused on the potential risks to individuals who would be handling contaminated products. The analyses of these human health risks show that acute risks to humans at the cross contamination levels allowed by this interpretation are negligible. Although intermittent contamination is the most likely scenario for cross contamination, it is possible that the same AI contaminant would be present in a particular pesticide product over a long period of time. EPA analyses indicate that chronic exposure to cross contamination is unlikely to present an unreasonable risk to human health.

EPA also considered contamination in pesticides applied to the human body (e.g., insect repellents) and concluded that the risks from cross contamination at the level set in this notice for these pesticides are negligible.

Adulterated food. Theoretically, a contaminant could cause residues in food or feed for which no tolerance has been established or that are in excess of an established tolerance. In this case, that food or feed would be adulterated under the Federal Food, Drug, and Cosmetic Act. EPA's analysis indicates that this is a highly unlikely occurrence. Moreover, because cross contamination with a specific AI occurs intermittently and at low levels, EPA believes that potential exposure to and dietary risk from residues of unreported contaminants under this notice would be negligible.

Ground water. The possibility of the contamination of ground water was raised as a potential concern in locations with sandy soils and shallow aquifers. The Florida Department of Agriculture and Consumer Services (DACS) conducted a preliminary ground water modeling exercise using a number of conservative assumptions regarding leachability, pesticide half-life, and product application rate. EPA accepts the Florida DACS conclusion that, while contamination of ground water is possible, it is of minimal concern

because pesticide AIs as contaminants at the levels allowed by this notice are unlikely to move to ground water in concentrations that would pose significant risk to human health.

Ecological effects/phytotoxicity. Based on a preliminary review of potential ecological effects from cross contamination (e.g., risks to birds, aquatic organisms, and plants), EPA believes that plant toxicity, or phytotoxicity, is the most sensitive endpoint given the relatively low concentrations of contaminants being considered. EPA believes that phytotoxicity damage poses the greatest potential for ecological harm. EPA's phytotoxicity analyses focus on the direct application of the contaminated product to terrestrial plants because this scenario represents a higher level of exposure than other exposure pathways, such as runoff and off-target drift.

EPA conducted several risk analyses based upon phytotoxicity as the end point of concern to determine the appropriate toxicologically significant levels. These analyses are presented in a technical support document. (See section VII on how to obtain more information.)

Rationale for not including certain microbial and biochemical pesticides and plant-pesticides. Many microbial and certain biochemical pesticides are manufactured in fermentors. A likely source of contamination of these pesticide products arises when a fermentor is used also for the production of a different microbial pesticide active ingredient. Quantitative criteria are not appropriate for determining whether active microbial pesticide ingredients are contaminants of 'toxicological significance'. This is because microorganisms can multiply in the environment, and especially in association with target pest hosts. The criteria of from 20 ppm to 1000 ppm as "toxicologically significant levels" (Section IV) when applied to a microbial pesticide active ingredient could allow for the presence of thousands to millions of contaminating microorganisms per gram or milliliter of pesticide product. It cannot be assumed that such levels of contamination are of insignificant toxicity, especially to non-target organisms.

EPA is in the process of developing policy for regulatory oversight of plant-pesticides, including defining the scope of oversight. Therefore, any determination of whether the quanti-tative criteria for toxicological significance apply to plant pesticides should be made once the plant-pesticide rule is finalized. Where applicants/registrants voluntarily submit plant-pesticides for EPA regulation, the reporting as discussed in Section V of this Notice will remain applicable unless otherwise changed by regulation.

IV. TOXICOLOGICALLY SIGNIFICANT LEVELS OF CONTAMINATION

The following table defines the levels of contaminants that EPA generally considers to be toxicologically significant. Specifically, the presence of a contaminant at a concentration greater than the concentration specified in the table will generally be considered toxicologically significant. Each contaminant should be considered individually.

The toxicologically significant levels apply to all registered products that are sold or distributed, regardless of whether the container is nonrefillable (i.e., "packaged product") or refillable (i.e., "bulk product.") The toxicologically significant levels do not apply to products that are not sold or distributed, such as tank mixtures in an end user's application equipment.

Toxicologically Significant Levels of Contaminants(1,2)

Category	Type of Contaminant	Type of Pesticide that is Contaminated	Toxicol. Significant Level(3) (ppm)(4)
1	Insecticide(5), fungicide, molluscide, or nematicide in...	Any insecticide, fungicide, molluscide, nematicide, herbicide, plant growth regulator, defoliant, or desiccant	1000
2	Herbicide, plant growth regulator, defoliant, or desiccant in...	Any pesticide(6) where the contaminant is accepted for use on all sites for which the product is labeled	1000
3	Any pesticide(6) other than a low application rate	An antimicrobial pesticide	1000

	herbicide(7) in...		
4	Normal rate herbicide(8), plant growth regulator, defoliant, or desiccant in...	Any herbicide, plant growth regulator, defoliant, or desiccant	250
5	Any pesticide(6) in...	A pesticide(6) applied to the human body	100
6	Normal rate herbicide, plant growth regulator, defoliant, or desiccant in...	Any insecticide, fungicide, molluscide, or nematicide	100
7	Low application rate herbicide in...	A low application rate herbicide	Level of quantification(9) or 100 ppm, whichever is higher
8	Low application rate herbicide in...	A normal rate herbicide, plant growth regulator, defoliant, or desiccan	Level of quantification(9) or 20 ppm, whichever is higher
9	Low application rate herbicide in...	A pesticide(6) other than a herbicide, plant growth regulator, defoliant, or desiccant	Level of quantification(9) or 1 ppm, whichever is higher

Notes:
(1) For the purposes of this notice, a contaminant is defined as an AI that is not on the product's confidential statement of formula or listed in the discussion of impurities.
(2) The following contamination scenarios are excluded from this notice: (a) rodenticides as a contaminant and/or as the contaminated product; (b) microbial and biochemical pesticides that are manufactured in fermentors and that are contaminated by active microbial pesticide ingredients; and (c) plant-pesticides that are contaminated with other active plant-pesticide ingredients. EPA would like to clarify that the Agency's previous position on toxicologically significant levels of impurities that are also AIs would apply pesticides that are exempt from this notice. In other words, any level of a contaminant in these three exempted scenarios would be considered potentially toxicologically significant and would have to be reported to EPA.
(3) This column presents the toxicologically significant level, i.e., the concentration at or above which EPA would consider the contaminant to be toxicologically significant.
(4) The concentration is determined in ppm based on the ratio of the weight of the contaminant to the weight of the formulated product.
(5) The FIFRA definition of insect includes mites and other arthropods that are not classified by scientific nomenclature as "insects." See FIFRA section 2(o).
(6) The phrases "any pesticide" and "a pesticide" do not include the pesticides that are specifically exempt from this notice as described in note #2 above.
(7) For the purposes of this notice, a low application rate herbicide is defined as a herbicide with a maximum labeled application rate of AI less than or equal to 0.5 pounds AI/acre. This definition is intended to include products with AIs that are amino acid inhibitors or ALS inhibitors, including but not limited to the sulfonylureas, imidazolinones, and triazolopyrimidines. (8) For the purposes of this notice, a normal rate herbicide is defined as a herbicide with a maximum labeled application rate of AI greater than 0.5 pounds AI/acre.
(9) For purposes of this notice, the level of quantification is the level of quantification achievable by EPA or its designated representative (State Lead Agency) using an analytical method suitable for enforcement purposes at the time the analysis is performed.

For categories 7, 8 and 9, the level of quantification is included in the table because EPA does not currently have analytical methods to detect and quantify these AIs in other products at concentrations as low as 100 ppm for category 7 (or lower for categories 8 and 9). EPA does not want to set a standard it cannot enforce. Conversely, EPA does not want to set a standard that constantly changes over time as analytical methods are continuously refined. Therefore, the standard of category 7 is the level of quantification until the point in time when the quantification limit drops below 100 ppm. The standard would then be 100 ppm, which is the limit based on toxicological significance. For purposes of this notice, the level of quantification is the level of quantification achievable by EPA or its designated representative (State Lead Agency) using an analytical method suitable for enforcement purposes at the time the analysis is

performed.

In selecting the levels in the table, EPA attempted to strike a reasonable balance between greater protectiveness and cost/burden considerations. If future experience indicates that these values are not sufficiently protective, the Agency may find it appropriate to modify these levels of toxicological significance.

EPA believes the values in the table are generally protective in most contaminant/product combinations. Because it is impracticable to consider every potential contaminant/product permutation, however, adverse effects could occur when contamination is present below the concentrations in the table.

The Agency recognizes that these standards will not prevent all possible adverse effects from occurring; this is not a zero risk standard. For example, EPA is aware of a situation where a normal rate herbicide contaminated an insecticide at levels below 100 ppm (as set out in Category 6) and plant damage occurred. The Agency will continue to deal with such situations using other regulatory tools including section 6(a)(2) of FIFRA.

Accordingly, this notice does not excuse applicants or registrants from the requirement to submit to EPA factual information regarding unreasonable adverse effects of a pesticide under section 6(a)(2) of FIFRA and EPA regulations at 40 CFR 152.50(f)(3). If an applicant or registrant possesses factual information not previously reported to EPA indicating that a contaminant in a product may pose risk to human health or the environment in concentrations lower than those specified in the above table, that information must be submitted to EPA. Failure to submit such information on a timely basis is a violation of sections 12(a)(2)(B)(ii) and 12(a)(2)(N) of FIFRA. In addition, the distribution or sale of any product containing an unreported contaminant that exceeds the levels identified in this notice is a violation of section 12(a)(1)(C) (composition differs) of FIFRA.

V. WHAT REGISTRANTS MUST DO

A. CONTAMINANT LEVEL EQUAL TO OR GREATER THAN THE TOXICOLOGICALLY SIGNIFICANT LEVEL

If an applicant or registrant knows or has reason to believe that a contaminant that EPA would consider toxicologically significant (i.e., an AI at a concentration equal to or greater than the appropriate level in the table) may be present, s/he must then include an expanded discussion of the possible formation of the impurity and the amounts at which it might be present in accordance with 40 CFR 158.167(c). EPA would then make a regulatory decision on whether to approve the registration or amendment to allow the sale and distribution of the product under FIFRA. Sale or distribution of a pesticide which equals or exceeds the toxicologically significant level prior to EPA approval of the registration amendment would be a violation. Reporting would be required regardless of where the contamination would be expected to occur in the production and distribution processes. As noted in the preamble to the regulations at 40 CFR 158.167, formulators utilizing registered materials are not required to seek information on the identity or level of impurities in the registered technical products they purchase. The Agency realizes that such information may not be made known to the formulator.

To submit an expanded discussion in accordance with 40 CFR 158.167(c), an applicant or registrant must provide EPA with (1) the identity of the contaminant and (2) the concentration at which it might be present. The information should be sent to EPA as follows.

For US Postal Service submissions:

Document Processing Desk (PM Team #)
Office of Pesticide Programs (7504C)
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460-0001.

For courier deliveries:

Document Processing Desk (PM Team #)
Office of Pesticide Programs (7504C)
U.S. Environmental Protection Agency
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202-4501.

B. CONTAMINANT LEVEL LESS THAN THE TOXICOLOGICALLY SIGNIFICANT LEVEL

If an applicant or registrant knows or has reason to believe that a contaminant may be present at a concentration that is less than the toxicologically significant level, s/he is not required to report this information to EPA. Please note that if a product is distributed or sold with levels of contamination that are equal to or exceed the toxicologically significant level, the product is in violation of FIFRA, irrespective of the registrant's knowledge.

However, adverse effects could still occur below the "toxicologically significant" concentrations set out in this notice. Registrants are reminded that they are responsible for reporting any adverse effects under FIFRA section 6(a)(2). Specifically, if an applicant or registrant possesses factual information not previously reported to EPA indicating that a contaminant in a product may pose risk to human health or the environment in concentrations lower than those specified in the above table, that information must be submitted to EPA. Failure to submit such information on a timely basis is a violation of sections 12(a)(2)(B)(ii) and 12(a)(2)(N) of FIFRA.

This notice is not intended to relieve registrants from liability that may exist under State law resulting from damage caused by contaminants.

As noted above, this notice is intended to inform registrants of the interpretation of the term "toxicologically significant" that the Agency intends to apply in implementing the provisions of 40 CFR Part 158. It is not intended, nor can it be relied upon, to create any rights enforceable by any party on litigation with the United States. EPA officials may act at variance with the guidance when circumstances indicate that a contaminant is of toxicological significance at levels different from those set forth in this notice.

EPA will take any regulatory action necessary to ensure that the levels of contamination in a product do not cause unreasonable adverse effects to human health or the environment.

VI. EFFECTIVE DATE

This notice is effective immediately.

VII. FURTHER INFORMATION

The public comments received on the proposed interpretation, the comment summary and response document, and the technical support document for this notice are available in the public docket under document number "OPP-00424." The public docket is located at: Public Docket and Freedom of Information Section, Field Operations Division, Office of Pesticide Programs, U.S. Environmental Protection Agency (7506C), Room 1132, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, Virginia, 22202.

If you have questions about the implementation of this notice, please contact Jim Jones at (703) 308-8358.

Daniel M. Barolo, Director
Office of Pesticide Programs